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Effect of alterations in the acid-base equilibrium on the lead contents of the blood and the mineral contents of plasma and erythrocytes in normal persons.

by Frida Schmitt and Irmgard Röttger.

Deutsches Archiv Klinischer Medizin, 184: 286-295 (1939).

In the clinical evaluation of the symptoms of lead poisoning, as well as in their interpretation, the level of hemal lead has become increasingly decisive. In order to make comparison possible, it has been standardized in numerous analyses of normal persons. Attempts to heal plumbic disease by the removal of lead from the organism, i.e. by attempts at mobilization, have shown that the metabolic equilibrium is affected thereby, resulting in alterations in the hemal lead contents of varying degree. This effect may be caused by the dispensing of drugs, as well as by shifts in the acid-base equilibrium of the organism. Since, normally, the pH of the body may shift to the acid as well as the alkaline side due to corresponding nutrition, it seemed indicated to investigate the potential of fluctuation in the hemal lead contents in normal persons under these conditions, and, simultaneously, to include its "opponents" in the pattern of osmotic balance in our considerations. The factors to be considered in the sphere of plumbic influence are, first, the mineral metabolism of plasma and erythrocytes, and second, the acid-base equilibrium of the blood.

Precise measurements exist of the alterations in the hemal acid-base equilibrium in normal persons (1). They have been conducted with hourly intervals in the course of one day, between 8:30 a.m. and 6:30 p.m., in connection with normal nutrition and occupation of the tested individuals. It was determined that no characteristic changes occur in the acid-base balance in the course of one day. The magnitude of fluctuation in the acid-base equilibrium from hour to hour is peculiar to the pertinent individual, although the extent of hourly fluctuation may vary in the same person on different days. Generally speaking, the differences in fluctuation are small. If the acid-base balance is now shifted toward the acid side with ammonium chloride, or to the alkaline with sodium bicarbonate, it is seen in most cases that the lowest point in acidosis is reached in 3-4 hours, and that 2 hours later (within individual bounds, of course) recovery has occurred. Recovery, therefore, is more rapid than loss. In alkalosis, the typical course shows apical values already after 1-2 hours, followed by a drop of approximately 50% within the next few hours. Complete recovery occurs very slowly, often on the next day.

Numerous authors have observed a mobilization of lead by means of sodium bicarbonate or ammonium chloride. According to Aub et al. (2), Litzner, Weyrauch and Barth (3), Leschke (4), the elimination of lead in the urine is increased by sodium bicarbonate. According [illegible] Schmitt and Taeger (5), who observed 2 cases of chronic lead poisoning, [illegible]creased elimination of lead, as well as an elevation [illegible] the level of hemal [illegible] takes place. Aub et al. noted a strong mobilization [illegible] lead after acidifi[illegible]tion of the organism by means of the acids HCl and H_3PO_4 or ammonium chloride. These observations were also

made by Schmitt and Taeger in connection with the cases of lead poisoning mentioned above. It was determined further that chlorine increased in the plasma and erythrocytes in both cases; sodium, on the other hand, decreased in both fractions.

All of these observations were made with fasting patients and no information is given concerning the conditions a few hours after the dispensing of corresponding drugs. Assuming that the mobilization of lead is caused by the shift toward the acid or alkaline side, a moment in time must be fixed analytically in which the organism is in the strongest acid or strongest alkaline condition, in order to obtain a picture of the actual happenings. The fasting value of the following day already ought to be affected by balancing influences. Starting with these considerations, the test program was organized as follows:

Tests were conducted with normal persons. Two different tests groups were organized. One produced a daily profile, giving information about the shift of minerals between plasma and erythrocytes, including chlorine, sodium, calcium, potassium, phosphorus and lead. The other group was to give a perspective on the mineral conditions at the end of an acid-base period, i.e. the highest acid or basic phase. The patients received the acid fare for 3 days. After an interval of 1 day, basic food was dispensed for 3 days.

The food on acid days is constituted of the following:

Early morning: 50 g wheat bread, 200 ccm coffee. Breakfast: 50 g wheat bread, 50 g sausage, 100 ccm oatmeal soup. Noon: 25 g wheat bread, 60 g meat, 300 ccm oatmeal. Afternoon: 50 g wheat bread, 200 ccm coffee. Evening: 50 g wheat bread, 200 ccm coffee, 200 ccm oatmeal cereal. In addition, 4.4 g ammonium chloride daily.

The basic food:

Early morning: 200 ccm coffee with milk. Breakfast: 100 ccm milk. Noon: 300 ccm mashed potatoes, 200 g vegetables. Afternoon: 100 ccm milk. Evening: 200 ccm milk, 200 g mashed potatoes, 200 g vegetables. In addition, 20 g sodium bicarbonate daily. In the daily profile, blood is withdrawn on the 1st acid day and the 1st basic day: Fasting (prior to commencement), at 1 p.m. and 7 p.m. Blood was taken from the other group: Fasting (prior to commencement), after the 3rd acid day and the 3rd basic day, also fasting.

All in all, about 60 ccm blood were withdrawn each time and prevented from coagulating by immediate addition of novirudin. CO_2 absorption curves and the hematocrit were determined from whole blood. It was then centrifuged for ½ hour, and the plasma and erythrocytes were isolated according to F. Schmitt's method (6). The contents of chlorine in the incinerated plasma were determined by [illegible]gyi and Rusznyak's method. For the remaining determinations the plasma and erythrocytes were incinerated according to Tschopp. For the determination of chlorine in the erythrocytes, 2 ccm n/1 silver nitrate solution was added to the blood corpuscles prior to combustion by the indicated method. After being turned to ash, the chlorine contents of the red blood cells were found by Volhard's method. In order to conduct mineral analyses, the excess $AgNO_3$ in the erythrocytic ash solution was precipitated out with a

few drops of hydrochloric acid. Now the plasma and erythrocytes were subjected to following determinations: sodium after Gruber, potassium and calcium after Kramer and Tisdal, phosphorus after Samson. The determination of lead was conducted according to a modified Dithizon method (7).

The results obtained at the end of one acid and one basic period are listed in table 1. The table shows that a considerable liberation of lead has taken place in the plasma and erythrocytes by the acidification of the organism. It shows individual diversity in magnitude. In all cases an increase in chlorine is noted in the plasma as well as in the erythrocytes. A reliable relationship between the extent of chlorine increase and the amount of liberated lead cannot be ascertained, however. The level of calcium in the plasma is changeable on acid days, in the last two cases it dropped; in the first it rose insignificantly. The erythrocytic calcium showed identical action, but with greater divergence. The total plasmatic phosphorus regularly increased after acid fare, in the erythrocytes this occurred only in the 1st case; in the 2d and 3rd it remained unchanged. The sodium levels of the plasma after the 3rd acid day were higher than initial values. The erythrocytic sodium level was slightly elevated in the first two cases, but only trivially so; in the 3rd case it had dropped. The potassium contents of the plasma showed a tendency to decrease in the 1st and 3rd case; it remained unchanged in the 2d. The erythrocytic potassium values are considerably increased in the 1st case, less so in the 3rd, and slightly decreased in the 2d case. Concerning plasmatic lead, only a very slight change is noted after the 3rd basic day, in comparison with initial values; the erythrocytes, on the other hand, show considerable plumbic increases in all 3 persons, in part even manifold values. The chlorine levels of the plasma are partly somewhat higher than initially, in one case slightly lower. The sodium contents of the plasma in the last two cases are higher than initially; in the 1st case this is not true; in the erythrocytes it is higher in the 1st and 3rd case, considerably lower in the 2d. Neither potassium nor calcium values of the plasma and erythrocytes show uniform changes due to altered pH toward the alkaline side.

Table 2 shows the effect on whole blood. It reveals definite increases in chlorine, sodium and, especially, in lead in all cases after the acid days. The deviations of potassium, calcium and phosphorus are changeable. After the basic days the chlorine levels of the whole blood are slightly above the initial values, as are the sodium levels. Potassium, calcium and phosphorus again fail to show unequivocal reactions. The plumbic values are again distinctly elevated and frequently surpass the values commonly found in normal persons by several times.

Progression of the absorption curve
on the acid day.

	30 mm	70 mm
Fasting:	34.2 vol.% CO_2	39.94 vol.% CO_2
1 p.m.:	31.6 "	34.7 "
7 p.m.:	37.78 "	44.1 "

4 hours after the ingestion of ammonium chloride, a distinct shift of the acid-base equilibrium occurred toward the acid side; 5 hours later a value is obtained which is above the initial factor and shifted to the alkaline side.

Table 3 lists the analytical series of those test days. They invariably show an increase in chlorine in the plasma after 4 hours, abating after 5 additional hours; the rise persists in the last case. In the erythrocytes, chlorine after 4 hours also exceeds the initial value, and shows a considerable increase in the next few hours, with the exception of case 2. Plasmatic lead increases in all cases due to the shift to the acid side, shows variations after an additional 5 hours, then sinks, in the last two cases, to values below the initial level; in the first two cases the rise persists. The fluctuations in erythrocytic lead levels after 4 hours are considerable in all cases; they abate extensively toward evening, with the exception of case 3, in which the lead level of the erythrocytes remains at approximately the same height. The sodium contents of the plasma after 4 hours are lower than initially, but considerably higher at 7 p.m., with the exception of case 3. Concerning the 4-hour level, erythrocytic sodium reveals the opposite reaction compared to plasma, i.e. the erythrocytic sodium increases, and this continuously until the end of the test. Potassium fails to show unequivocal reactions in the plasma or in the erythrocytes. Calcium levels in the plasma had a tendency to rise during the course of the day, while falling in the erythrocytes. Similarly, no system could be deduced from the total phosphorus of both fractions.

Table 4 offers a perspective on the shift in minerals in the whole blood during the test days. It discloses an increase in chlorine and lead in all cases after 4 hours. In 3 cases the chlorine level rises until evening, while a drop is evidenced by case 2. The lead contents of whole blood at 7.p.m. are still above those of the initial stage, but lower than the 4-hour values.

Progression of the absorption curve
on the basic day.

	30 mm	70 mm
Fasting:	36.9 vol.% CO_2	51.82 vol.% CO_2
1 p.m.:	44.2 "	70.59 "
7 p.m.:	42.1 "	62.08 "

It is noted that a shift in the acid-base equilibrium toward the alkaline side has taken place after 4 hours; further, that the alkaline shift continues to persist, although not at as high a level as at 1 p.m.

Table 5 indicates mineral movement on the basic day. It is evident, in most cases, that the plasmatic chlorine has dropped at 1 p.m. At this time, all cases reveal a considerable decrease in erythrocytic chlorine. The lead contents of the plasma have increased only insignificantly after 4 hours; the erythrocytic lead is distinctly increased. Chlorine in the plasma fluctuates, it generally decreases somewhat in comparison to 4-hour values. Erythrocytic chlorine levels are above those of the 4-hour point, in some cases even above initial values. The level of lead in the plasma is significantly higher than initial and 4-hour values in one case only. In the other cases it is only

slightly above the starting value. The lead contents of the erythrocytes are also higher than corresponding fasting values, but only in 2 cases higher than at the 4-hour point. Plasmatic potassium increases in the course of the day; calcium after 4 hours, decreasing thereafter in most cases. Erythrocytic potassium is variable, calcium drops in most cases after 4 hours and rises later, but usually not to the initial level. Sodium increases after 4 hours in the plasma as well as in the erythrocytes, and as a rule decreases somewhat toward evening. Phosphorus levels in the plasma rise toward 1 p.m. and , in one case, also toward 7 p.m. No uniform reaction is indicated in the erythrocytes.

The whole blood (table 6) is affected as follows by the basic day: Here, too, a distinct drop in chlorine is seen after 4 hours, followed by rising levels. With the exception of case 3, sodium and chlorine actions are analogous. The actions of potassium, calcium and phosphorus are not uniform. Whole blood lead increases after 4 hours and continues to rise until evening in cases 1 and 3, while a decrease in the lead contents of the blood is noted in cases 2 and 4.

Discussion of the results.

Our experiments were able to confirm findings by earlier writers, to the effect that a change in pH of the organism toward the alkaline or acid side, extending over several days, leads to the mobilization of lead. It can further be deduced from our tests that the liberation of lead in the plasma is greater after acid periods than after basic ones, while the opposite is true for erythrocytes. In the plasma, the shift of lead progresses in the same manner as that of chlorine, i.e. both increase after acid days and decrease after the basic period; these two phases of movement cross in the erythrocytes. This regularity cannot be found in whole blood. Acid days lead to rises in chlorine and lead. Basic days bring a drop in chlorine and, again, increased lead values in the blood. Both processes of mobilization usually yield plumbic values in excess of the norm.

During the course of an acid day, considerable quantities of lead are released into the blood, the greatest liberation of lead coinciding with the strongly acid pH of the organism; while the shift of chlorine in the erythrocytes (in isolated cases also in the plasma) takes a different course, i.e. it continues to increase. In whole blood, the highest plumbic values also coincide with the lowest position of the CO_2 absorption curve. They usually l[illegible] above the values which we still classify as normal; the fluctuations are individual, however. At times values are found that amount to double the norm.

The release of lead into the plasma is low in the course of a basic day. Divergences are more pronounced in the erythrocytes, but they do not attain the levels observed on acid days. The hemal lead level of the erythrocytes continues to show higher values compared to acid days. This agrees with the action of the acid-base equilibrium which returns [illegible] more slowly to the norm from alkaline pH than on acid days. The plumbic level of whole blood shows only one case in which the value is considerably above normal. A relationship between hemal lead and the remaining ions cannot be deduced with certainty.

Aerobiology Div
Mrs. J. R. Riley

#210
Cy. 1

Effect of alterations in the acid-base equilibrium on the lead content of the blood and the mineral content of plasma and erythrocytes in normal persons.

by Frida Schmitt and Irmgard Röttger.

Deutsches Archiv Klinischer Medizin, 184: 286-295 (1939). (Summary and tables only).

Summary.

To reiterate: A shift in the acid-base equilibrium of the organism toward the acid or alkaline side evokes the mobilization of lead, even in healthy persons. The activation of lead is greater toward the acid side than toward the alkaline. On acid days, the movement of chlorine and lead is found to be uniform, while the decrease in chlorine is matched by an increase in lead on basic days, leading to the assumption that the mobilization of lead represents a function of the change in pH. Acid as well as basic days yield concentrations of lead in excess of the norm.

It is significant in the daily profile of the acid days that the highest values of lead coincide with the lowest position of the curve representing carbonic acid fixation. The activation of lead occurring on a basic day is also dependent on the change in pH. The gradual return of alkalosis to the norm is accompanied by a gradual decrease in the hemal lead content.

Here, too, greater amounts of lead are mobilized by an acid pH than by alkaline.

These tests have shown how readily the hemal lead content is changed by relatively trifling operations, even in lead-free persons. For the practical evaluation of the level of hemal lead, this circumstance reveals that "increased" values do not necessarily reflect a plumbic disease, but may be an expression of corresponding mutrition or therapy. This consideration should in all cases be included in an evaluation of the level of lead in the blood.

Input on acid days.

Early morning: 50 g wheat bread, 200 ccm coffee. Breakfast: 50 g wheat bread, 50 g sausage, 100 ccm oatmeal soup. Noon: 25 g wheat bread, 60 g meat, 300 ccm oatmeal. Afternoon: 50 g wheat bread, 200 ccm coffee. Evening: 50 g wheat bread, 200 ccm coffee, 200 ccm oatmeal cereal. In addition, 4.4 g ammonium chloride daily.

Input on basic days.

[illegible] morning: 200 ccm coffee with milk. Breakfast: 100 ccm milk. Noon: [illegible] ccm mashed potatoes, 200 g vegetables. Afternoon: 100 ccm milk. Evening: 200 ccm milk, 200 g mashed potatoes, 200 g vegetables. In addition, 20 g sodium bicarbonate daily.

Table 1.

Bo. — Bo. (name) prior to commencement
n. ̲ — after 3 acid days
n. 3.B. — after 3 basic days
Gesamtblut Hämatokrit — whole blood hematocrit.

Table 2.

Gesamtblut — whole blood.

Table 3.

Tagesprofil — daily profile
Stü. nü. — Stü. (name) fasting
13 Uhr — 1 p.m.
19 Uhr — 7 p.m.
Gesamtblut Hämatokrit — whole blood hematocrit

Table 4.

Sauertag — acid day
Tagesprofil — daily profile
Gesamtblut — whole blood.

Table 5.

Basentag — basic day
Tagesprofil — daily profile
Gesamtblut Hämatokrit — whole blood hematocrit.

Table 6.

Basentag — basic day
Tagesprofil — daily profile
Gesamtblut — whole blood.